

Sub B contd
A18
Cont.

stings/bites, herpetic infections, systemic sclerosis, morphoea, dermal nodular fibrosis or sunburn.

22. A method according to Claim 15 wherein the skin disease or condition is, has been or will be further treated by application of a corticosteroid.

Sub C7
23. A composition as in any of Claims 1 to 12 being adapted to treat a patient in need of said polar drug by applying said composition to the skin of the patient.

Sub C8
A19
28. The composition of any one of Claims 1 to 12 being packaged in a tube, tub, bottle or pressurised aerosol container.

29. A composition according to any one of Claims 1 to 12 being adapted for use in medicine.

Remarks

The Examiner states that the Oath or Declaration filed with the present application is defective for showing an incorrect filing date. However, the filing date of November 21, 2000 shown in the Declaration is indeed correct. The original Filing Receipt from the USPTO indicated an incorrect filing date of February 1, 2001. As a result, a Request for Corrected Filing Receipt was submitted to the USPTO on March 1, 2001. A Corrected Filing Receipt indicating the correct filing date of

November 21, 2000 was subsequently issued by the USPTO. Copies of the relevant documents are enclosed herewith.

A new Declaration in compliance with 37 C.F.R. §1.67(a) reflecting the correct chain of priority is currently awaiting execution by the inventor. The new executed Declaration will be forwarded to the USPTO as soon as possible. The new Declaration correctly identifies the PCT parent application as PCT/GB99/01600, and the prior foreign application upon which priority is claimed as GB9810949.9, filed May 22, 1998.

The Examiner's comments regarding the use of trademarks in the specification have been noted and addressed. The proper use and accompanying generic terminology has been inserted into the specification.

Claims 1, 3-5, 9, 10, 12, 13, 15, 17, 20-23, 28, and 29 have been amended. Claims 2, 6-8, 14, 16, 18, 19, and 24-27 have been cancelled. Claims 1, 3-5, 9-13, 15, 17, 20-23, 28, and 29 remain in the application. Consideration and allowance of these claims as now presented is respectfully requested.

Claim Objections

The claim objections under 37 C.F.R. §1.75(c) for multiple dependency have been addressed as requested by the Examiner.

Rejection of Claims Under 35 U.S.C. §112

Claims 3, 4, 5, 16, 18-22, and 24-27 stand rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out the subject matter of the invention.

The Examiner asserts that the term "balanced" in Claim 3 is an indefinite term. However, the term "balanced" is well known to those skilled in the art, as shown, for example, by Martindale The Complete Drug Reference, 32nd Ed, page 1468. In addition, the specification at page 8, lines 20-27 defines the term "balanced" with reference to surfactants. As particularly stated therein, "[I]f the isoelectric point of the molecule occurs at pH 7, the molecule is said to be balanced". Therefore, Applicant submits that the term "balanced", as used in Claim 3, is sufficiently defined so as to be understood by one of ordinary skill in the art. Thus, the rejection of Claim 3 under 35 U.S.C. §112 should accordingly be withdrawn.

The remaining claim rejections under §112 have been addressed by amending the claims as suggested by the Examiner. As such, the rejections under 35 U.S.C. §112 should accordingly be withdrawn.

Rejection of Claims Under 35 U.S.C. §102

Claim 14 stands rejected under 35 U.S.C. §102(b) as being anticipated by Kjellman et al. Claim 14 has been cancelled thereby obviating the rejections thereon.

Rejection of Claims Under 35 U.S.C. §103

Claims 1-3 and 14-16 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Totten et al. (GB2202145) and Kjellman et al. in view of Murad (U.S. 6,071,541) or Letini et al. (U.S. 6,177,092).

Neither of the cited references Murad '541 nor Letini et al. '092 are available as prior art against the present application. The present United States national application is a national phase filing of PCT application PCT/GB99/01600. The PCT application from which the present national phase application was spawned claims priority from British patent application Serial No. 9810949.9, filed May 22, 1998. Copies of relevant application papers claiming priority from British application 9810949.9 are enclosed herewith. As stated above, a new Declaration for the present application correctly identifying the priority documents will be filed with the USPTO as soon as possible.

The effective filing date of the present application, therefore, is the filing date of British patent application 9810949.9, which is May 22, 1998. The earliest priority

date for Letini et al. '092 is the filing date of November 10, 1998. The earliest priority date for Murad '541 is the filing date of related provisional application no. 60/094,775, which was filed on July 31, 1998. 35 U.S.C. §365(b) provides that an international application designating the United States shall be entitled to the right of priority of a prior foreign application, which may either be another international application or a regularly filed foreign application. 35 U.S.C. §365(b) applies to the present application, as it is a national phase application of an international application designating the United States. Therefore, the effective filing date of the present application for right of priority is May 22, 1998. Thus, the present application pre-dates the cited references Murad '541 and Letini et al. '092, and, as such, neither Murad '541 nor Letini et al. '092 may be cited as prior art in the present case. As a result, the asserted claim rejections under 35 U.S.C. §103(a) are inoperative, and should accordingly be withdrawn.

Even if the asserted claim rejections were operative, the cited prior art fails to teach or suggest the invention as presently claimed. The presently pending claims recite a composition and use thereof comprising a polar drug selected from the group consisting of sodium cromoglycate

and nedocromil, an alkoxyated cetyl alcohol, and an amphoteric surfactant. As stated, for example, at page 5, lines 4-24 of the application as originally filed, the presently claimed composition displays unexpectedly beneficial effects in the treatment of skin disease such as atopic dermatitis. In particular, the present application discloses the unexpected beneficial effect of combining an alkoxyated cetyl alcohol and an amphoteric surfactant as a useful and effective combination for delivering the selected polar drug to a targeted area in the skin of a patient. No teaching of such beneficial effects of combining an alkoxyated cetyl alcohol and an amphoteric surfactant into a skin disease treatment substance along with a selected polar drug is found in the cited prior art. As such, there is no motivation or suggestion to combine the cited references as done here by the Examiner. Therefore, the claim rejections under 35 U.S.C. §103(a) should accordingly be withdrawn.

For the foregoing reasons, the claims as presently amended are believed to be unobvious and patentable over the cited prior art, whether taken alone or in combination. Applicants therefore submit that the claims as currently presented are allowable on the merits. An early allowance is respectfully solicited.

Respectfully submitted,

HAUGEN LAW FIRM PLLP

A handwritten signature in black ink, appearing to read "Mark J. Burns", written over a horizontal line.

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Version with Marking to Show Changes Made

In the Specification

Please insert the following amended paragraphs in place of the respective previous version paragraphs.

Beginning with page 12, lines 5-12:

The term alkoxylated cetyl alcohol encompasses polypropoxylated cetyl alcohol, the chemical description given for Procetyl AWS™ in *Gardner's Chemical Synonyms and Trade Names*, ninth edition. Alkoxylated cetyl alcohol may be obtained from Croda Chemicals Ltd., Cowick Hall, Snaith, Goole, North Humberside, DN14 9AA. It is marketed as "Procetyl AWS™". The alkoxylated cetyl alcohol may be useful for its water soluble surface active emollient properties. It may also act as an emulsifying and solubilising agent and imparts a silky feel to the skin.

Page 14, lines 13-29:

The oil phase may comprise liquid paraffins, white soft paraffin, glycerol monostearate, non-ionic emulsifying wax or a lipophilic non-ionic surfactant (for example sorbitan tristearate), benzyl alcohol and/or isopropyl myristate. These terms are well known to those skilled in the art. Isopropyl myristate is an example of an emollient. Glycerol monostearate is an example of an emulsifying agent and may also act as an emollient. Benzyl

alcohol is an example of a preservative and a mild local anaesthetic. The non-ionic emulsifying wax may be Polawax NF™ (a blend of higher fatty alcohols and polyoxyethylene sorbitan fatty acid ester, in particular a blend of cetostearyl alcohol and sorbitan tristearate). Non-ionic emulsifying wax may be useful in the preparation of emulsions comprising polar substances. A lipophilic non-ionic surfactant, for example sorbitan tristearate, may be used as an alternative to or in addition to a non-ionic emulsifying wax. Liquid paraffins and isopropyl myristate may act as emollients and form an occlusive film on the skin as water dries away from the emulsion. This film may assist in keeping the skin hydrated from the water applied in the emulsion.

Page 15, lines 14-23:

The nonionic emulsifying wax, for example Polawax NF™, or lipophilic non-ionic surfactant, for example sorbitan tristearate, may provide from 0.1 to 15% w/v, preferably 0.5 to 5% w/v, still more preferably about 2% w/v of the emulsion. It is preferred that a lipophilic non-ionic surfactant, for example sorbitan tristearate, provides from 0.5 to 5% w/v of the emulsion or that the nonionic emulsifying wax, for example Polawax NF™, provides from 2 to 5% w/v. It will be appreciated that if the nonionic

emulsifying wax, for example Polawax NF™ provides more than about 5% of the emulsion that the resulting emulsion may be too viscous to spread easily on the skin.

Page 17, lines 12-16:

Sorbitan tristearate may be obtained under the name Crill 35™ from Croda Chemicals Limited, Cowick Hall, Snaith, Goole, North Humberside DN14 9AA. Polawax NF™ may also be obtained from Croda Chemicals Limited. It is preferred that Polawax NF™ is used in preference to sorbitan tristearate (Crill 35™).

Page 18, line 27:

sorbitan tristearate or non-ionic emulsifying wax
(Polawax NF™), 1.3%

Page 20, lines 22-26:

It may be necessary to select patients on the basis of the level of circulating IgE. Suitable IgE tests include an *in vitro* total IgE test and an *in vitro* specific IgE test, for example the UniCAP Total (or Specific) IgE tests sold by Pharmacia & Upjohn, which use the Allergen InnumunoCAPS™ as the allergen reagent.

Page 24, lines 6-20:

The cromone and corticosteroid may be presented in the same formulation or in separate formulations. The cromone and corticosteroid may be presented as separate

formulations for topical application. Either or both formulations (if appropriate) may be a composition, for example an emulsion, of the invention. As described in Examples 3 and 4, a formulation comprising a corticosteroid may be applied before or after (preferably before) a formulation of the invention comprising a cromone for example sodium cromoglycate. The corticosteroid may be in a polar or a non-polar form; preferably it is in a non-polar form if it is not presented in a composition of the invention. Suitable formulations comprising a non-polar corticosteroid include the proprietary formulations Betnovate RD™ (bethamethasone valerate, ready diluted), Aureocort™ (triamcinolone acetonide and chlortetracycline hydrochloride (an antibiotic)), and Eumovate™ (clobetasone butyrate). A 1% hydrocortisone preparation may also be used.

Page 27, line 29:

sorbitan tristearate or Polawax NF™ 2.0%

Page 29, line 25:

Polawax NF™ 2.0%

Page 30, line 2:

Miranol™ 2.0%

Page 30, line 3:

Procetyl AWS™

In the Claims

Please cancel Claims 2, 6-8, 14, 16, 18-19, and 24-27.

Please amend Claims 1, 3-5, 9-10, 12-13, 15, 17, 20-23, 28 and 29 as follows.

Claim 1 (Amended). A composition comprising an amphoteric surfactant, an alkoxyated cetyl alcohol and a polar drug selected from the group consisting of sodium cromoglycate and nedocromil sodium.

Claim 3 (Amended). A composition according to Claim 1 [or 2] wherein the amphoteric surfactant is a balanced amphoteric surfactant.

Claim 4 (Amended). A composition according to Claim 1 [any of the preceding claims] wherein the alkoxyated cetyl alcohol is polypropoxylated cetyl alcohol [Procetyl AWS].

Claim 5 (Amended). A composition according to Claim 1 [any of the preceding claims] wherein the amphoteric surfactant comprises disodium cocoamphodiacetate [coacoamphodiacetate].

Claim 9 (Amended). A composition according to Claim 1 [6] wherein the composition further comprises a corticosteroid.

Claim 10 (Amended). A composition according to Claim 1 [any of the preceding claims] wherein the composition comprises an aqueous phase and an oil phase.

Claim 12 (Amended). A composition according to Claim 1 [any of the preceding claims] wherein the composition is a foam.

Claim 13 (Amended). A composition according to any of the preceding claims consisting substantially of:

sorbitan tristearate or non-ionic emulsifying wax 0.5 to 5% w/v

glycerol monostearate	0.5 to 5% w/v
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light liquid paraffin	1 to 20% w/v
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white soft paraffin	1 to 10% w/v
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iso propyl myristate	0.5 to 5% w/v
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<u>polar drug</u>	0.1 to 20% w/v
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disodium edetate	0.01 to 1% w/v
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amphoteric surfactant	0.1 to 10% w/v
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alkoxylated cetyl alcohol	0.1 to 10% w/v
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triclosan	0.01 to 1% w/v
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benzyl alcohol	0.01 to 1% w/v
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purified water	to 100% of the emulsion
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Claim 15 (Amended). A method for treating [of treatment of] a skin disease or condition, comprising: [wherein a]

(a) providing a polar drug selected from the group consisting of sodium cromoglycate and nedocromil sodium; and

(b) applying said polar drug [is applied] to the skin of an individual affected by the disease or condition

in or with a formulation comprising alkoxyated cetyl alcohol and an amphoteric surfactant.

Claim 17 (Amended). A composition as in Claim 1 that is useful for [method of] treatment of a skin disease or condition [comprising] by applying said [a] composition [or emulsion according to any one of Claims 1 to 14] to the skin of an individual affected by the disease or condition.

Claim 20 (Amended). A method as in Claim 15 [Use according to Claim 18 or 19] wherein the disease or condition is one in which skin mast cells and/or delayed [(cellular)] hypersensitivity reactions and/or inflammation is thought to be involved.

Claim 21 (Amended). A method as in Claim 15 [Use according to any one of Claim 18 to 20] in which the disease or condition is atopic dermatitis or eczema, contact sensitivity, psoriasis, drug sensitivity reactions, apthous ulcers, Behcet's syndrome, pemphigus, urticaria, urticaria pigmentosa, pyroderma gangrenosum, chronic skin ulcers, ulcers associated with Crohn's disease, burns, insect stings/bites, herpetic infections, systemic sclerosis [(systemic scleroderma)], morphoea [(circumscribed or localised scleroderma)], dermal nodular fibrosis or sunburn.

Claim 22 (Amended). [The use according to Claim 16, 18, to 21 or] A method according to Claim 15 [or 17] wherein the skin disease or condition is, has been or will be further treated by application of a corticosteroid.

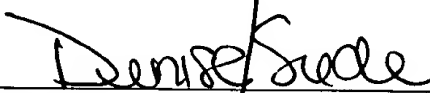
Claim 23 (Amended). A composition as in any of Claims 1 to 12 being adapted to treat [method of treatment of] a patient in need of said [a] polar drug [comprising] by applying said [a] composition [or emulsion according to any one of Claims 1 to 13 comprising the said polar drug] to the skin of the [said] patient.

Claim 28 (Amended). The composition [or emulsion] of any one of Claims 1 to 12 being [14] packaged in a tube, tub, bottle or pressurised aerosol container.

Claim 29 (Amended). A composition [or emulsion] according to any one of Claims 1 to 12 being adapted [14] for use in medicine.

CERTIFICATE OF MAILING

I hereby certify that the foregoing Amendment in application Serial No. 09/701,140, filed November 21, 2000 of Brian Hawtin, entitled "FORMULATION", together with a transmittal cover letter a corrected, unexecuted Declaration and copies of the Filing Receipt, Requested for a Corrected Filing Receipt and the Corrected Filing Receipt are being deposited with the United States Postal Service as First Class mail, postage prepaid, in an envelope addressed to: The Commissioner of Patents and Trademarks, Washington, D. C. 20231, on this 24th day of April, 2002.



Denise L. Siede
Secretary to Mark J. Burns
Attorney for Applicants

Date of Signature: April 24, 2002